

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Schena, Mark A.
 Assignee: TeleChem International Inc.
 Title: Microarray Method Of Genotyping Multiple Samples At Multiple Loci
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San Jose, California

BOX RCE
 COMMISSIONER FOR PATENTS
 Washington, D. C. 20231

DECLARATION OF LINDA C. FOSTER PURSUANT TO 37 C.F.R. §1.132

Dear Sir:

Linda C. Foster declares and states as follows:

1. I have 20 years of experience as a chemical and biological scientist in the biopharmaceutical industry. After graduating from U.C. Berkeley (B.Sc. Chemistry) in 1982, I worked at Syntex as a physical organic chemist to optimize chemical structure with biological activity for a number of drugs in development. I subsequently worked at California Biotechnology (now Scios) and Inhale Therapeutic Systems. In the latter positions I expanded my expertise in small molecule compounds to macromolecules, drug delivery devices, and drug discovery systems. At Inhale Therapeutic Systems I was Director of Research. In 1998 I left Inhale to co-found Aura Oncology Systems, where I am currently Chairman of the Board.

2. I am named as an inventor on 13 issued patents that span a range of scientific disciplines including macromolecule formulation and stabilization, amorphous solid state and powder chemistry, drug delivery, and vaccine adjuvants. I have contributed to the development of various small molecule drugs that are currently on the market, including

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Gancyclovir (an antiviral nucleotide), Aleve (Naprosyn, an NSAID), Lidex (steroid), Ticlid (cardiovascular antiplatelet agent); Toradol (NSAID for pain relief from bone surgery); Cardene (calcium beta blocker); and CellCept (tissue rejection).

3. In the course of my research and development work, I have developed extensive experience working with small molecules and macromolecules used by the biotechnology and pharmaceutical industry and knowledge of how synthetic oligonucleotides are prepared and used.

4. In the chemical and biological sciences, it is understood by those of ordinary skill that the term "synthetic oligonucleotide" refers exclusively to oligonucleotides prepared by chemical synthesis.

5. In the chemical and biological sciences, those of ordinary skill would not understand the term "synthetic oligonucleotide" to refer to oligonucleotides prepared by means other than chemical synthesis. For example, those of ordinary skill in the chemical and biological sciences would not understand the term "synthetic oligonucleotide" to refer to oligonucleotides or oligomers made enzymatically.

6. Those of ordinary skill in the chemical and biological sciences would not regard cDNA and genomic DNA to be "synthetic oligonucleotides."

7. Consequently, those of ordinary skill in the chemical and biological sciences would understand that, in a genotyping method, the "synthetic oligonucleotides" employed in an act of "hybridizing the microarray with a mixture of labeled synthetic oligonucleotides" are chemically synthesized oligonucleotides rather than oligonucleotides prepared by means other than chemical synthesis. For example, those of ordinary skill in the chemical and biological sciences would not understand the "synthetic oligonucleotides" employed in the act of "hybridizing the microarray with a mixture of labeled synthetic oligonucleotides" to be oligonucleotides prepared enzymatically or, in particular, to be cDNA or genomic DNA.

8. I have reviewed the three definitions of "synthetic" provided in the Academic Press Dictionary of Science and Technology (Morris, C. ed., Academic Press, 1992, page

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2157) and corresponding, respectively, to the fields of "science," "chemistry," and "engineering." A copy of the page including the three definitions is attached to this declaration.

9. A definition of "synthetic oligonucleotide" constructed by juxtaposing the term "oligonucleotide" with the "chemistry" definition of "synthetic" provided in the Academic Press Dictionary of Science and Technology would be equivalent to the meaning of "synthetic oligonucleotide" as it is understood by those of ordinary skill in the chemical and biological sciences.

10. A definition of "synthetic oligonucleotide" constructed by juxtaposing the term "oligonucleotide" with the "engineering" definition of "synthetic" provided in the Academic Press Dictionary of Science and Technology would not be equivalent to the meaning of "synthetic oligonucleotide" as it is understood by those of ordinary skill in the chemical and biological sciences.

11. A definition of "synthetic oligonucleotide" constructed by juxtaposing the term "oligonucleotide" with the "science" definition of "synthetic" provided in the Academic Press Dictionary of Science and Technology would be equivalent to the meaning of "synthetic oligonucleotide" as it is understood by those of ordinary skill in the chemical and biological sciences only if "synthesis" were understood to refer to chemical synthesis.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Linda C. Foster
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Date



Academic Press Dictionary of Science and Technology

Edited by
Christopher Morris



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synoptic wave chart *Oceanography.* a chart of an area that shows synchronous wave reports from vessels and other sources, as well as predicted wave heights for areas not reported on; may also have wave-height isolines drawn in, along with meteorological data.

synoptic weather observation *Meteorology.* a periodic surface weather observation of sky cover, state of the sky, cloud height, sea-level atmospheric pressure, temperature, dew point, wind speed and direction, precipitation, and any special phenomena that are present at the time of the observation or that have been observed since the previous observation; as specified by the World Meteorological Organization, such observations usually occur at regular three- and six-hour intervals.

synochidism *Medicine.* a fusion of the testes. Also, *synorchism*.

synorogenic *Geology.* describing a geologic process or event that took place at the same time as a mountain-building event, or a rock or feature formed during that time.

synostosis *Anatomy.* 1. the osseous union of adjacent bones or adjacent parts of a single bone that were separated by fibrous or cartilaginous material before they were joined. 2. the osseous union of bones that are normally distinct. Also, *synosteosis*.

synovial fluid *Physiology.* the transparent liquid produced by the synovial membranes of a joint, and acting as a lubricant. Also, *synovia*.

synovial joint see *DIARTHRYSIS*.

synovial membrane *Histology.* a layer of connective tissue that lines joint cavities, bursae, and tendon sheaths. The membrane produces synovial fluid that has a lubricating function.

synovioma *Medicine.* a tumor originating in the synovial membrane.

synoviosarcoma *Oncology.* a malignant neoplasm in the synovial membrane contained in joint cavities, bursae, and tendon sheaths.

synovitis *Medicine.* an inflammation of a synovial membrane, usually as the result of an aseptic wound or an injury, characterized by swelling due to the accumulation of fluid around the capsule; the joint is tender and painful, and motion is restricted.

synpeltous *Vertebrate Zoology.* having the two main flexor tendons of the toes united beyond the branches to each digit, as in certain birds.

synphylogeny *Ecology.* the science or study of the historical and evolutionary trends and changes that take place within plant communities.

synphysiology *Ecology.* the science or study of the evolutionary trends and changes that take place within plant communities.

synsepalous see *GAMOSEPALOUS*.

syntactic [sin'tak'tik] *Linguistics.* having to do with syntax. Also, *syntactical*.

syntactic ambiguity *Artificial Intelligence.* the possibility that a natural-language sentence can be parsed in more than one way; e.g., "I saw John's dog driving to work today."

syntactic analysis *Computer Science.* 1. a compilation step that includes lexical analysis, statement parsing, and intermediate code generation. 2. the parsing of a language to generate a parse tree. Also, *SYNTAX ANALYSIS*.

syntactic extension *Computer Programming.* a feature of an extensible language that permits the definition of new notations for existing or user-defined mechanisms.

syntactics *Linguistics.* the branch of semiotics that deals with the formal characteristics of symbols and signs.

syntax [sin'taks] *Linguistics.* 1. the set of natural rules or patterns that govern how message-bearing units (i.e., words and word parts such as prefixes) are combined in a language to form meaningful sentences. 2. the study of these rules or patterns. *Artificial Intelligence.* a formal statement of the grammatically acceptable forms of a natural language; used in language analysis. *Computer Programming.* a set of rules specifying the structure of a programming language.

syntax analysis see *SYNTACTIC ANALYSIS*.

syntax checker *Computer Programming.* a program that tests source statements in a programming language for violations of its syntax. Also, *SYNTAX SCANNER*.

syntax diagram *Computer Programming.* a diagram representing the structural rules of a programming language.

syntax-directed compiler *Computer Programming.* a compiler whose activities are based on syntactical relations found in parsing the input program. Also, *syntax-oriented compiler*.

syntax-directed translation *Computer Science.* the translation of a statement, for example, in a programming language, that is guided by the syntactic form of the statement.

syntax-directed translator *Computer Science.* a program, such as a compiler, that performs translation from a language into another form in a syntax-directed manner.

syntax error *Computer Programming.* a violation of the grammatical rules of a programming language statement, such as misspelling the name of a command. Also, *syntactic error*.

syntaxial overgrowth *Mineralogy.* an optically oriented crystal overgrowth on a detrital mineral grain of identical composition, formed during diagenesis.

syntax scanner see *SYNTAX CHECKER*.

syntechny *Ecology.* a resemblance between unrelated organisms due to their adaptation to similar environments. Thus, *syntechnic*.

syntectic *Geology.* describing a magma formed by the melting of two or more rock types and the assimilation of country rock.

syntectonic *Geology.* describing a process, event, or geological feature that occurred or was formed during any kind of tectonic activity. Also, *SYNINEMATIC*.

Syntelidae *Invertebrate Zoology.* the sap-flow beetles, a superfamily of coleopteran insects in the superfamily Histeroidea.

syntenic genes *Genetics.* genes that are thought to be located on the same chromosome because they are lost concurrently with a specific marker gene that is known to be located on that chromosome.

synteny *Genetics.* the condition of genetic loci that lie on the same chromosome.

Syntexidae *Invertebrate Zoology.* a family of wasps, hymenopteran insects in the superfamily Siricoidea, having a single species *Syntexis libocedrii*; larvae are found in North American incense cedars.

syntexis *Geology.* a process by which magma is generated by the melting of two or more rock types and the assimilation of country rock.

synthase see *LYASE*.

synthesis [sin'tha sis] *Science.* 1. the combining of constituent elements into a unified entity. 2. a unified whole formed by combining. *Chemistry.* specifically, the process of building chemical compounds from more elementary substances by means of one or more chemical reactions, or by nuclear change. *Control Systems.* the use of available components to plan and construct a system that will perform in a specified manner. Also, *SYSTEM DESIGN*.

synthesis gas *Chemical Engineering.* a mixture of hydrogen and carbon monoxide obtained by the reforming of methane. Also, *SYNGAS*.

synthesis of continuity *Surgery.* the union of the edges of a wound or the ends of a fractured bone.

synthesize [sin'tha siz'] *Chemistry.* to carry on a process of synthesis; form a single or unified entity from constituent elements.

synthesized attribute *Computer Science.* an attribute of a structure, e.g., a phrase in a programming language statement, that is derived from the attributes of its components. For example, the sum of two floating-point quantities will also be floating point.

synthesized translation *Computer Science.* a method of translating statements, e.g., in a programming language, such that the translation of a phrase is built up from the translations of its components.

synthesizer *Electronics.* 1. any of various instruments that integrate simple elements or functions to produce more complex entities. 2. specifically, an electronic device that simulates the sound of various musical instruments.

synthetase see *LIGASE*.

synthetic *Science.* relating to, produced by, or involving synthesis. *Chemistry.* relating to compounds formed artificially by chemical synthesis. *Engineering.* in general, describing any product or item that is the result of human technology rather than something that exists in nature.

synthetic aperture *Engineering.* a technique by which the phase relationship of two receiving systems, such as radar receivers or telescopes, is used to emulate the resolving power of an instrument having an aperture equal to their separation.

synthetic aperture radar *Engineering.* a radar technique in which a timed pulse signal is sent out from an aircraft flying a very steady course; the phase of returned pulses is analyzed to emulate the characteristics of a radar with an antenna size of up to a mile.

synthetic basic motion times *Industrial Engineering.* standard time values that are obtained from predetermined systems or that are determined by measuring similar task elements, rather than by directly measuring the work at hand, because they apply to basic motions that are common to many tasks. Also, *BASIC MOTION TIMES*.

synthetic detergent *Materials.* any synthetic substance other than soap that is an effective cleanser and functions equally well as a surface-active agent in hard or soft water.

synthetic diet *Biochemistry.* a diet that consists only of known chemical ingredients.

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